The Rupe Reaction applied to 3-(n-Perfluorobutyl)alk-2-yn-1-ols: an Unexpected Route to 5-n-Perfluoropropylfuran-3(2*H*)-ones

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Under the conditions of the Rupe reaction hydration of the triple bond of the perfluorobutylalkynols n-$C_4F_9C{\equiv}CCR(Me)OH$ occurs yielding the ketone n-$C_4F_9CH_2COCR(Me)OH$; this ketone undergoes intramolecular reaction providing an interesting route to 5-n-perfluoropropylfuran-3(2*H*)-ones.

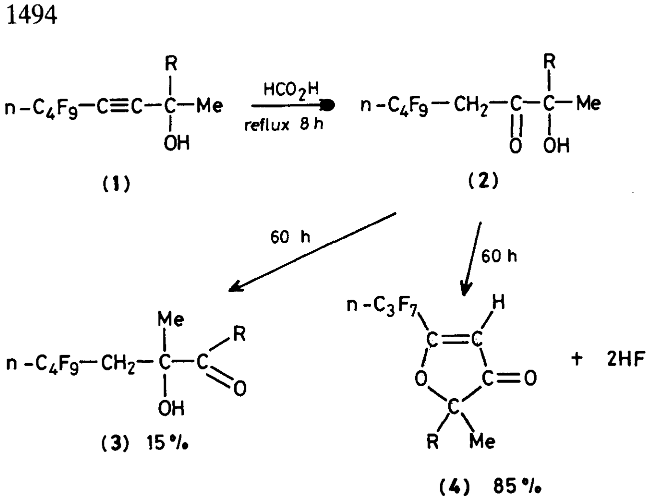
The rearrangement of α-ethynyl alcohols to unsaturated carbonyl compounds under the conditions of the Rupe reaction, reflux with formic acid, has been studied in detail.[1] The results show that in general dehydration of the alcohol function and hydration of the triple bond occurs.

Studying this reaction using the 3-(perfluorobutyl)alk-2-yn-1-ols[2] n-C_4F_9–$C{\equiv}C$–$CR(Me)OH$, we observed different results. Formation of the formate occurs rapidly, which is unusual for tertiary alcohols (30% after 1 h). We do not observe any dehydration of the alcohol even when R = Et, in contrast with the case of the non-fluorinated analogues.[1]

Hydration of the triple bond occurs only at the acetylenic carbon without the perfluoroalkyl group, and is complete after 8 h. The ketones obtained are present as alcohols (**2**) and formates (ratio 4 : 6) and give rise to the acyloin rearrangement.[3] Only 7% of the ketones (**2**) are transposed into (**3**), after 24 h of reaction, 15% after 60 h (Scheme 1).[†]

Further reaction leads to a new compound, in 85% yield after 60 h, identified as the 2-methyl-2-alkyl-5-perfluoropropylfuran-3(2*H*)-one (**4**). A possible mechanism for the formation of this compound is shown in Scheme 2.

[†] The alcohols are mixed with formic acid (molar ratio 1 : 20) and heated at reflux. The different alcohol : acid ratio from the reactions of the non-fluorinated analogues (ref. 1) is necessary because of miscibility problems. H_2O necessary for the hydration reaction comes from residual H_2O in the acid (2%) and from the esterification reaction. Yields are relative to the starting alcohol. The more usual Rupe reagent of 80% acid, 20% H_2O was not used because of the limited solubility of the fluoroalkynol used. Instead acid containing 2% H_2O was used.



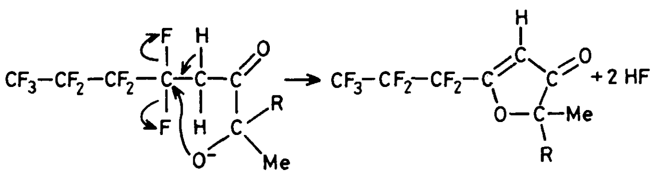
R = Me, Et

Scheme 1

The liberated HF is clearly detected in the ^{19}F n.m.r. spectrum of the medium.‡ This intramolecular reaction demonstrates the assistance of the CF_2 group in a nucleophilic attack. The conversion of (**2**) into (**4**) is rapid (<1 h) and clean in a basic medium (KOH–MeOH).

However, whilst the oxygen-centred anion may be involved in attack on the CF_2 group under basic conditions, this route seems unlikely in an acid medium. Additional work is necessary to clarify the mechanism of the formation of (**4**) in such a medium. A possible sequence of reactions is (i) HF elimination from (**2**), not favoured in acid medium, but possible. (ii) Protonation of the carbonyl group and formation of a positive charge on the carbon atom of the –CF= terminal group through a mesomeric equilibrium. Cyclisation and HF elimination leads to (**4**).

The basic route is rapid and quantitative in the formation of (**4**) from the starting alcohol, but the acid-catalysed route is a



Scheme 2

one pot experiment with 85% yield in (**4**), the remaining 15% being the α-hydroxy ketone (**3**).

It is of interest, from a mechanistic point of view to compare the observed reaction with other methods of synthesis of furan-3(2*H*)-ones: the hydration of but-2-yne-1,4-diols,[4] and more interesting the acid-catalysed cyclisation–dehydration of an appropriately substituted α′-hydroxy-1,3-diketone,[5] this last route being the most efficient approach to the furan-3(2*H*)-one ring system.

The reactions observed provide a simple route to 5-perfluoropropylfuran-3(2*H*)-ones, a class of compounds whose synthesis has commanded considerable attention.[4–6]

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‡ All the compounds described have been identified using ^{1}H, ^{19}F, and ^{13}C n.m.r., i.r., and mass spectral analysis.